

Agency was sufficient to establish that the products were intended to affect the structure or function of the body. FDA last considered whether cigarettes were drugs or devices in the late 1970's, determining that the limited evidence then before the Agency was insufficient to demonstrate that these products were intended to affect the structure or function of the body. *See Action on Smoking and Health v. Harris*, 655 F.2d 236 (D.C. Cir. 1980). Since that time, substantial new evidence has become available to FDA. This evidence includes the emergence of a scientific consensus that cigarettes and smokeless tobacco cause addiction to nicotine and the disclosure of thousands of pages of internal tobacco company documents detailing that the manufacturers intend to affect the structure and function of the human body.

The determination whether a product is subject to FDA jurisdiction often requires the Agency to make difficult factual judgments, including judgments regarding the intended use of the product. The Agency must have enough evidence to show that these factual judgments are rational and not "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. 706(2)(A); *see National Nutritional Foods Ass'n v. Weinberger*, 512 F.2d 688, 700-701 (2d Cir. 1975), *cert. denied*, 423 U.S. 827 (1975). The Agency must provide some evidentiary support for its factual judgments, and there must be a rational connection between these judgments and the conclusions reached. *Motor Vehicle Mfrs. Ass'n of the United States, Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 42-43 (1983). The Agency should also have considered all the relevant data and the relevant aspects of the issue. *Id.*; *Citizens to Preserve Overton Park, Inc. v. Volpe*, 401 U.S. 402, 416 (1971). An agency's factual judgments made in the context of an informal agency action ordinarily need only be supported by a record that

shows a “rational basis” for the agency’s decision, *Natural Resources Defense Council, Inc. v. EPA*, 16 F.3d 1395, 1401 (4th Cir. 1993), or by a record consisting of “some evidence” in support of the agency’s decision. *Aman v. FAA*, 856 F.2d 946, 950 n.3 (7th Cir. 1988) (while an agency determination need only have “some evidentiary basis to avoid being held ‘arbitrary and capricious,’ [t]he difference between ‘some’ and ‘substantial’ probably cannot be precisely stated except in the context of particular cases. . . .”). Several courts, however, have held that an agency’s factual judgments must always be supported by “substantial evidence,” even though that standard is intended to be applied only to formal “on the record” agency actions, *see* 5 U.S.C. 706(2)(E).<sup>1</sup>

In this case, the Agency’s evidentiary record exceeds these standards. That is, FDA has concluded that the evidence now before the Agency supports a finding of jurisdiction over these products. In assessing the new evidence, FDA has used a two-step approach, evaluating first whether the nicotine in these products “affects the structure or

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<sup>1</sup> *See, e.g., Ass’n of Data Processing Service Organizations, Inc. v. Board of Governors*, 745 F.2d 677, 683-684 (D.C. Cir. 1984) (Scalia, J) (“When the arbitrary or capricious standard is performing that function of assuring factual support, there is no substantive difference between what it requires and what would be required by the substantial evidence test, since it is impossible to conceive of a ‘nonarbitrary’ factual judgment supported only by evidence that is not substantial in the APA sense . . . .”). *Contra Corrosion Proof Fittings v. EPA*, 947 F.2d 1201, 1213-1214 and n.17 (5th Cir. 1991) (declining to find that the substantial evidence standard and the arbitrary and capricious standard “are in fact one and the same”); *Am. Paper Inst. v. Am. Elec. Power Serv. Corp.*, 461 U.S. 402, 412 n.7 (1983) (in the absence of a specific command in the statute to employ a particular standard of review, the Court of Appeals should have applied the more lenient arbitrary and capricious standard in evaluating the factual basis supporting an agency’s informal rulemaking).

The difference in the case law, however, is of no consequence here because FDA’s evidentiary record exceeds the “substantial evidence” standard—the more stringent of the two standards. Substantial evidence is “such relevant evidence as a reasonable mind might accept as adequate to support a conclusion,” *Consolo v. Federal Maritime Commission*, 383 U.S. 607, 619-620 (1966) (quoting *Consolidated Edison Co. v. NLRB*, 305 U.S. 197, 229 (1938)), even if two inconsistent conclusions might be inferred from the same evidence. *See Consolo*, 383 U.S. at 620; *NLRB v. Nevada Consolidated Copper Corp.*, 316 U.S. 105, 106 (1942). Under the substantial evidence standard, an agency’s factual determinations are conclusive even if supported by “something less than the weight of the evidence . . . .” *Consolo*, 383 U.S. at 620 (emphasis added).

any function of the body” and second whether these effects are “intended.” FDA has determined that the evidence overwhelmingly demonstrates that (1) nicotine in cigarettes and smokeless tobacco has significant effects on the structure and function of the body and (2) these effects are intended by the manufacturers of these products.

The Agency’s determination that nicotine in cigarettes and smokeless tobacco “affect[s] the structure or any function of the body” is based on three central findings:

1. Nicotine in cigarettes and smokeless tobacco causes and sustains addiction.
2. Nicotine in cigarettes and smokeless tobacco causes other psychoactive (mood-altering) effects, including tranquilization and stimulation.
3. Nicotine in cigarettes and smokeless tobacco controls weight.

These findings demonstrate that nicotine in cigarettes and smokeless tobacco has the same pharmacological effects as other drugs that FDA has traditionally regulated, including tranquilizers, stimulants, appetite suppressants, and products used in the maintenance of addiction such as methadone. Thus, the effects of nicotine in cigarettes and smokeless tobacco on the structure and function of the body are within FDA’s jurisdiction.

FDA’s determination that the manufacturers of cigarettes and smokeless tobacco “intend” the effects of nicotine on the structure and function of the body is based on five central findings:

1. The addictive and other pharmacological effects of nicotine are so widely known and accepted that it is foreseeable to a reasonable manufacturer that cigarettes and smokeless tobacco will cause addiction to nicotine and other significant pharmacological effects and will be used by

consumers for pharmacological purposes, including sustaining their addiction to nicotine.

2. Consumers use cigarettes and smokeless tobacco predominantly for pharmacological purposes, including sustaining their addiction to nicotine, mood alteration, and weight loss.
3. Manufacturers of cigarettes and smokeless tobacco know that nicotine in their products causes pharmacological effects in consumers, including addiction to nicotine and mood alteration, and that consumers use their products primarily to obtain the pharmacological effects of nicotine.
4. Manufacturers of cigarettes and smokeless tobacco design their products to provide consumers with a pharmacologically active dose of nicotine.
5. An inevitable consequence of the design of cigarettes and smokeless tobacco to provide pharmacologically active doses of nicotine is to keep consumers using cigarettes and smokeless tobacco by sustaining their addiction to nicotine.

Each of these findings provides an independent basis for establishing that the manufacturers of cigarettes and smokeless tobacco “intend” to affect the structure and function of the body. Taken together, the cumulative weight of the evidence convincingly supports the determination that the effects of nicotine on the structure and function of the body are “intended” by the manufacturers.

FDA’s assertion of jurisdiction over cigarettes and smokeless tobacco is consistent with the Agency’s assertion of jurisdiction over other similar products. FDA regulates a diverse range of products under the Act. These products—foods, drugs, devices, cosmetics, and radiation-emitting electronic products—all “affect the health and well-being of the public.” *United States v. Park*, 421 U.S. 658, 672 (1975). The common feature that distinguishes these products is their intimate and potentially harmful contact

with the human body. *See id.* at 668. FDA-regulated products include those that are intended to be ingested, inhaled, applied to the skin, implanted, or otherwise used in close contact with the body. Cigarettes, which deliver a pharmacologically active dose of nicotine to the body through inhalation, and smokeless tobacco, which delivers a pharmacologically active dose of nicotine through buccal absorption, share this distinguishing feature and thus are properly subject to FDA jurisdiction.

The determinations that (1) the nicotine in cigarettes and smokeless tobacco “affects the structure or any function of the body” and (2) these effects are “intended” by the manufacturers satisfy the legal requirements under the Act for FDA jurisdiction. FDA has also determined that cigarettes and smokeless tobacco contain both a “drug” and a “device” and are thus combination products within the meaning of the Act. Accordingly, the Agency has concluded that the nicotine in cigarettes and smokeless tobacco is a drug and that cigarettes and smokeless tobacco are drug delivery devices under the Federal Food, Drug, and Cosmetic Act.

I.

**I. CIGARETTES AND SMOKELESS TOBACCO “AFFECT THE STRUCTURE OR ANY FUNCTION OF THE BODY” WITHIN THE MEANING OF THE ACT**

In the Jurisdictional Analysis, FDA found, based on the evidence available to it at the time, that nicotine in cigarettes and smokeless tobacco is “highly addictive, causes other psychoactive effects, such as relaxation and stimulation, and affects weight regulation.” *See* Jurisdictional Analysis, 60 FR 41464 (Aug. 11, 1995). The Agency found that the nicotine in these products “has pharmacological effects on both the structure and function of the central nervous system, particularly the brain,” and that “[a]ddiction is a direct result of nicotine’s effects on the structure and function of the body.” *Id.* at 41470. Based on these findings of pharmacological effects, the Agency found that cigarettes and smokeless tobacco “*affect the structure or any function of the body.*” *Id.* (emphasis added).

As described more fully below, the Agency received comments that agreed and disagreed with the Agency’s position.<sup>2</sup> After considering the evidence in the administrative record,<sup>3</sup> including the public comments, the Agency finds that cigarettes and

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<sup>2</sup> The Agency received a consolidated comment of the cigarette industry (Brown & Williamson Tobacco Corp., Liggett Group Inc., Lorillard Tobacco Co., Philip Morris Inc., R.J. Reynolds Tobacco Co., Tobacco Institute Inc.) (Jan. 2, 1996) (hereinafter Joint Comments of the Cigarette Manufacturers). *See* AR (Vol. 535 Ref. 96). The Agency also received a consolidated comment of the smokeless tobacco industry (Smokeless Tobacco Council Inc., Brown & Williamson Tobacco Corp., Conwood Co., L.P., National Tobacco Co., L.P., the Pinkerton Tobacco Co., R.C. Owen Co., Swisher International, Inc., United States Tobacco Co.) (Jan. 2, 1996) (hereinafter Joint Comments of the Smokeless Tobacco Manufacturers). *See* AR (Vol. 526 Ref. 95).

<sup>3</sup> In the footnotes of this document, cites to the administrative record (AR) specify both the number of the reference and the volume of the AR in which the reference is found. The reference may contain the full document or a partial document. Where the reference contains a partial document, the full document may be found elsewhere in the AR. In a small number of cases, a reference will occupy several volumes of the AR, for example, the Joint Comments of the Cigarette Manufacturers. In these cases, the cite will specify the volume of the AR in which the reference begins.

## I.A.

smokeless tobacco do indeed “affect the structure or any function of the body” within the meaning of sections 201(g)(1)(C) and 201(h)(3) of the Act, 21 U.S.C. 321(g)(1)(C), 321(h)(3).

To interpret the Federal Food, Drug, and Cosmetic Act in a manner that excludes the effects of these products from the scope of the structure-function prong of the drug and device definitions would be inconsistent with the plain meaning of the Act, its legislative history, case law interpreting the structure-function prong, and the Agency’s past applications of that provision. The Agency’s conclusions are summarized in section I.A., followed by a detailed discussion of the comments and the Agency’s responses to them in section I.B.

**A. THE PHARMACOLOGICAL EFFECTS OF THE NICOTINE IN CIGARETTES AND SMOKELESS TOBACCO ON THE BODY ARE SIGNIFICANT**

Cigarettes and smokeless tobacco contain nicotine, an addictive and pharmacologically active drug. *See* section II.A., below. Nicotine is the active ingredient in several products regulated as drugs by the Agency, including nicotine transdermal patches, nicotine chewing gums, nicotine nasal spray, and Favor, a hollow paper tube with nicotine impregnated in the mouthpiece. *See* Jurisdictional Analysis, 60 FR 41482, 41549-41550. The effects of the nicotine in cigarettes and smokeless tobacco greatly exceed those exerted by the nicotine-containing products already regulated by the Agency.<sup>4</sup>

Nicotine in cigarettes and smokeless tobacco produces significant pharmacological effects on the human body. First, nicotine causes and sustains addiction. The processes

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<sup>4</sup> Nicotine-use cessation products are discussed in section II.A.5., below.

## I.A.

that lead to addiction to nicotine in cigarettes and smokeless tobacco are similar to those that lead to addiction to products such as morphine and opium. *See* section II.A.2., below. Like other addictive substances, nicotine in cigarettes and smokeless tobacco achieves its addictive effects by exerting psychoactive, or mood-altering, effects on the brain and by producing chemical reactions in the brain that motivate repeated, compulsive use of the substance. *See* section II.A.3., below. These pharmacological effects create dependence in the user. *Id.*

In addition to creating and sustaining addiction, cigarettes and smokeless tobacco produce other significant pharmacological effects. For example, under some circumstances, nicotine in cigarettes and smokeless tobacco has a sedating or tranquilizing effect on mood and brain activity. *See* section II.A.4., below. Under other circumstances, nicotine in cigarettes and smokeless tobacco has a stimulant or arousal-increasing effect on the body. *Id.*

Nicotine in cigarettes and smokeless tobacco also controls body weight. *Id.* Clinical and animal studies indicate that nicotine administration causes weight loss and that cessation of nicotine administration results in weight gain. *Id.*

These effects on the structure and function of the body are significant and quintessentially drug-like. They produce immediate pharmacological changes in the function of the brain (depressing or stimulating arousal); they change the physical structure of the body (increased growth of nicotine receptors in the brain, weight loss); and they cause drug dependence (addiction). *Id.*

## I.A.

The tobacco industry comments argue that “remote” or “insignificant” pharmacological effects are not subject to FDA jurisdiction. Although “remote physical effect[s] upon the body” may not be covered by the structure-function provision, *see E.R. Squibb & Sons, Inc. v. Bowen*, 870 F.2d 678, 682 (D.C. Cir. 1989), the pharmacological effects of cigarettes and smokeless tobacco are not “remote” or insignificant. Indeed, they are powerful and immediate pharmacological effects that are not qualitatively or quantitatively different from the effects of other drugs subject to FDA jurisdiction.

In fact, the effects of cigarettes and smokeless tobacco—addiction, sedation, stimulation, and weight loss—are precisely the types of effects the Agency traditionally regulates. It is well established that the Agency has the authority to regulate, and has regulated, products that sedate, tranquilize, or reduce anxiety (e.g., Valium and other benzodiazepines); products that stimulate or restore mental alertness (e.g., caffeine-containing pills such as NoDoz, *see Stimulant Drug Products for Over-the-Counter Human Use, Final Monograph*, 53 FR 6100 (February 29, 1988); 21 CFR Part 340);<sup>5</sup> products that cause weight loss (*see Weight Control Products for Over-the-Counter Human Use, Certain Active Ingredients*, 56 FR 37792 (August 8, 1991); 21 CFR 310.545(a)(20); *see also United States v. 354 Bulk Cartons . . . Trim Reducing-Aid Cigarettes*, 178 F. Supp. 847, 851 (D.N.J. 1959)); and products that are used for maintenance treatment of addiction (e.g., methadone and other “narcotic drugs [used] in the medical treatment of narcotic addiction,” 21 CFR 291.501). The approved uses of these products include uses to “affect the structure or any function of the body” under

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<sup>5</sup> A more detailed discussion of the Agency’s regulation of caffeine and caffeine-containing products is contained in section I.B., below.

I.A.

section 201(g)(1)(C) of the Act. Thus, cigarettes and smokeless tobacco have the same effects as products that are undeniably within FDA's jurisdiction.

Indeed, internal tobacco company documents reveal that tobacco industry scientists understand that the nicotine in tobacco produces pharmacological effects no different from those produced by approved drugs. These industry scientists viewed prescription drugs as competing products.<sup>6</sup> Over three decades ago, the British American Tobacco Company (BATCO), the parent of Brown & Williamson Tobacco Corporation, commissioned a study to compare the effects of nicotine with those of tranquilizers, "which might supersede tobacco habits in the near future."<sup>7</sup> The study concluded that nicotine was "more beneficial or less noxious—than the new tranquilizers" because it reduced stress and regulated weight.<sup>8</sup>

Philip Morris and R.J. Reynolds Tobacco Company (RJR) also have repeatedly compared the effects of nicotine from tobacco to the effects of drugs regulated by FDA. For example, Philip Morris researchers and officials have concluded that smokers use cigarettes as "a narcotic, tranquilizer, or sedative"<sup>9</sup> and that "[nicotine] is a physiologically active, nitrogen containing substance. *Similar organic chemicals include . . . quinine,*

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<sup>6</sup> These documents, and the conclusions the Agency has drawn from them, are described in detail in sections II.C. and II.D., below.

<sup>7</sup> Haselbach CH, Libert O, *Final Report on Project HIPPO II* (Geneva: Battelle Memorial Institute, International Division, Mar. 1963), at 1. See AR (Vol. 64 Ref. 321).

<sup>8</sup> *Id.* at 2.

<sup>9</sup> Udow A, *Why People Start to Smoke* (Jun. 2, 1976), in 141 Cong. Rec. H7664 (daily ed. Jul. 25, 1995). See AR (Vol. 14 Ref. 175a).